Human Pathology: Case Reports 5 (2016) 29–33

Contents lists available at ScienceDirect

Human Pathology: Case Reports

journal homepage: http://www.humanpathologycasereports.com

Giant seminoma case with very small yolk sac and embryo carcinoma components, detected by intensive histopathological examination

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ARTICLE INFO

Article history:
Received 30 August 2015
Received in revised form 26 October 2015
Accepted 29 October 2015

Keywords:
Giant seminoma
Yolk sac tumor
Embryo carcinoma
Intensive histological examination

ABSTRACT

We experienced the giant seminoma with 18 × 10 × 10 cm sized and about 2.6 kg weight of 25 year old patient. We intensively examined the histological tissue type distributions in this giant seminoma. Most of the tumor consisted of seminoma components. In addition, the tumor included the very small fragments of yolk sac tumor and embryonal carcinoma component at the root part of the seminoma mass. This shows that intensive histological examination may contribute to the finding of other embryonic component of the large seminoma. This may show that leaving the seminoma growing may generate the other embryonic tumor component, not always big enough to find out in a routine procedure, during the growth, in the different way from the original mixed cell germ tumor.

1. Introduction

Seminoma is a common germ cell tumor. Usually testicular tumors are found at earlier stages, because testes are visible from patients. Thus patients seldom let their seminoma grow into giant sized tumors. This makes it very difficult to follow the natural history of growth and development of seminoma in its original lesion.

Several giant testicular tumor cases have been reported [1–6]. According to the giant testicular tumor cases reported in Japan, 66% of the giant seminomas consisted of pure seminoma components, even in the very large seminomas over 8 kg [4]. In general, tumors have worse biological characters or worse elements as they grow larger, because of the accumulation of genetic changes during their growths [7]. We had the question whether so many seminomas consist of only pure classic seminoma component during the growth into giant size. It is difficult to distinguish different germinal cell tumor components from classic seminoma component macroscopically in the rather large proportion of giant seminomas. We speculate that this is the reason why so many giant seminomas were diagnosed as pure classic seminomas, by picking up smaller number of the blocks from the large specimens.

We experienced a giant seminoma case. In order to answer the above mentioned question, we performed the intensive histopathological examination (Fig. 1C). We detected the very small non-seminomatous components which might not be detected by the conventional histological examination of picking up smaller number of blocks.

This suggested a natural history of seminoma that the tumor initiating cells, which can differentiate into seminoma only, may change into the tumor initiating cells which can generate other types of germ cell tumors, some of them with much poorer prognoses, during the growth into large sized tumors.

2. Case report

2.1. Clinical history

25 year old male patient had suffered from the enlargement of his left testis for 3 years, but he had not visited a hospital for a long time. When he came our hospital for the first time, because of the fever, the testicular tumor developed into about 18 × 10 × 10 cm size. Blood test results were, WBC 18,900/μl, hCG 3300 IU/l, AFP 222.8 ng/ml, LDH 1732 U/l, just before the surgical operation. Computerized tomography (CT) detected the metastasis of the tumor in his para-aortic lymph nodes, but no metastasis was found in his lung. The high orchiectomy operation was performed and the giant seminoma was removed. The testicular tumor was diagnosed as stage IIA, intermediate risk, by the

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http://dx.doi.org/10.1016/j.ehpc.2015.10.005

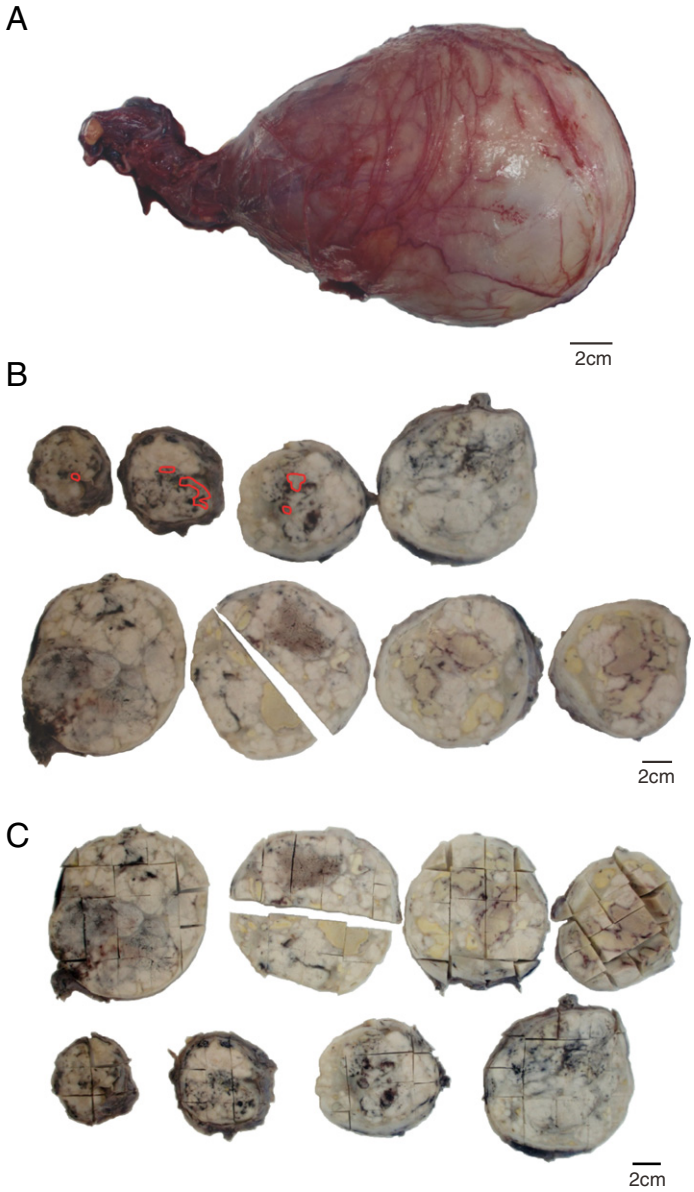

Fig. 1. A) Macroscopic view of the giant seminoma of 18 × 10 × 10 cm sized and about 2.6 kg weight. B) Macroscopic view of the sections of the giant seminoma. The red circled area includes yolk sac tumor and embryonal carcinoma components. The other areas are classic seminoma components. C) Intensive pathological examinations of the giant seminoma.

IGCCC classification of testicular tumors. Because the testicular tumor included non-seminomatous elements, VIP [VP-16 (etoposide) or vinblastine plus ifosfamide and cisplatin] therapy was selected as postoperative chemotherapy, according to the clinical guideline for testicular tumors. The para-aortic metastasis shrank and AFP score in his blood declined into normal range after the chemotherapy, by CT survey. Therefore the lymphadenectomy for retroperitoneal lymph nodes was not performed. The patient left the hospital, and he is now under good control of the testicular tumor for one year after the surgical operation.

2.2. Pathological findings

The tumor was 18 × 10 × 10 cm sized and about 2620 g weight (Fig. 1A). We dissected the tumor into the sections in the CT section. The tumor was composed of white and yellowish solid nodules with some hemorrhages and necroses (Fig. 1B). Among 157 blocks, 7 blocks included non-seminomatous elements in this large testicular tumor. Non-seminomatous elements occupied approximately 0.32% of this testicular tumor.

We made all the sections into the slides (157 blocks) and examined, and performed the histological examinations of all the slides (Fig. 1C).

Most of the tumor included classic seminoma component (Fig. 2A). Very small areas near the root of the tumor included the yolk sac tumor or embryonal carcinoma, as indicated in the red circulated area in Fig. 1B.

The tumor included yolk sac tumor component, with reticular structures (Fig. 2B). Schiller–Duval bodies were histologically unclear in the yolk sac tumor component, and alpha-fetoprotein (AFP) was immunohistochemically negative.

The embryonal carcinoma component with the tubular epithelial structure, was included in the giant tumor (Fig. 2C). Syncitiotrophoblastic cells with strong positive hCG were also detected in the tumor (Fig. 2D) [8].

The seminoma component was Oct4 positive and glypican 3 negative (Fig. 2E and F), yolk sac tumor component was Oct4 positive and

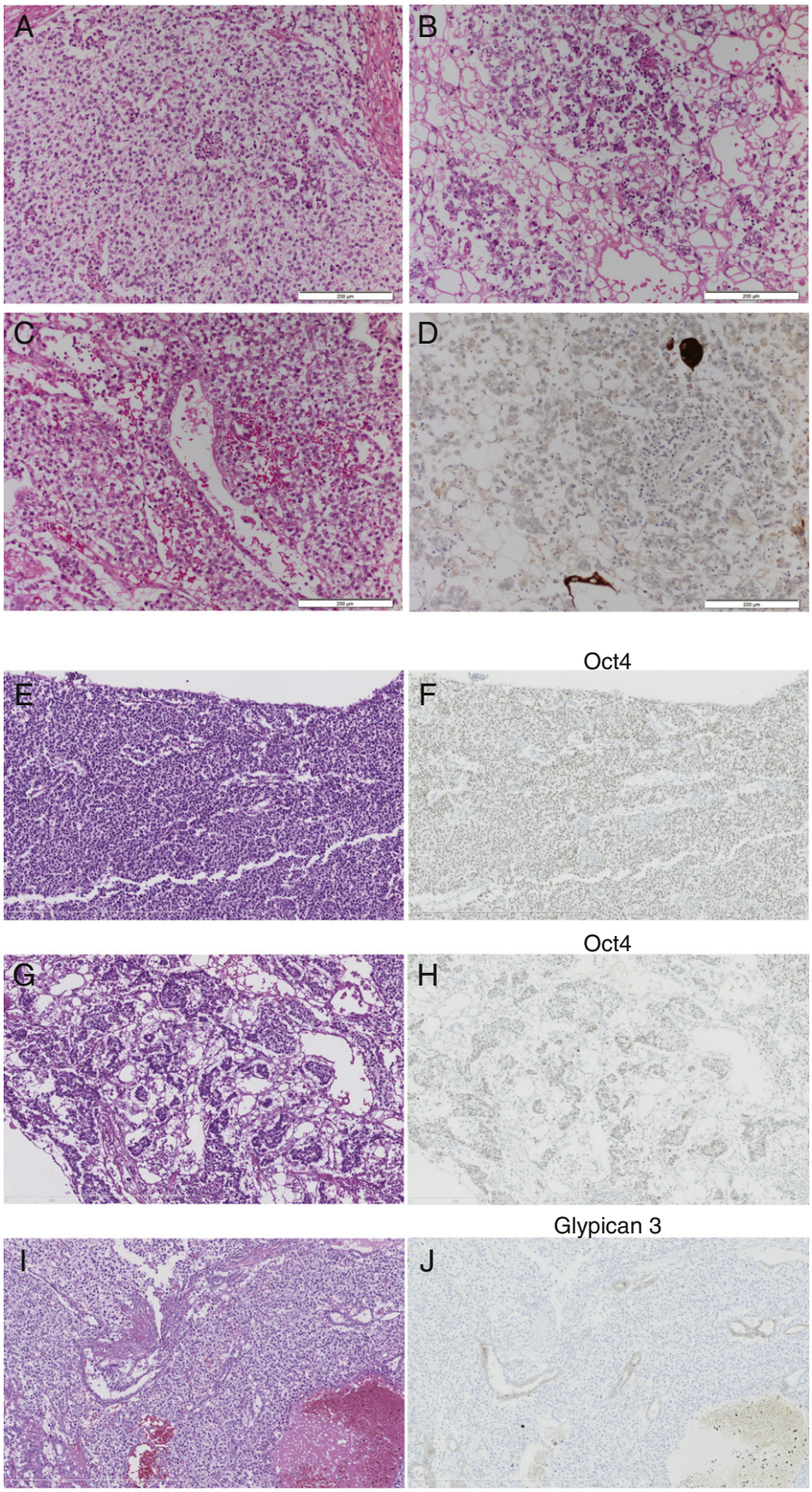

Fig. 2. A) Histological view of the classic seminoma of the giant seminoma. Most of the giant tumor composed of this classic seminoma. B) Histological view of the yolk sac tumor in the giant seminoma. The giant seminoma included very small yolk sac tumor component. C) Histological view of the embryonal carcinoma in the giant seminoma. The giant seminoma included very small embryonal carcinoma component, which included epithelial tubular components. D) Immunohistochemistry of hCG stains the syncytiotrophoblastic cells in the giant tumor. E and F) Immunohistochemistry of Oct4 stains the seminoma cells in the giant tumor. G and H) Immunohistochemistry of Oct4 stains the yolk sac tumor cells in the giant tumor. I and J) Immunohistochemistry of glypican 3 stains the embryonal carcinoma cells in the giant tumor.

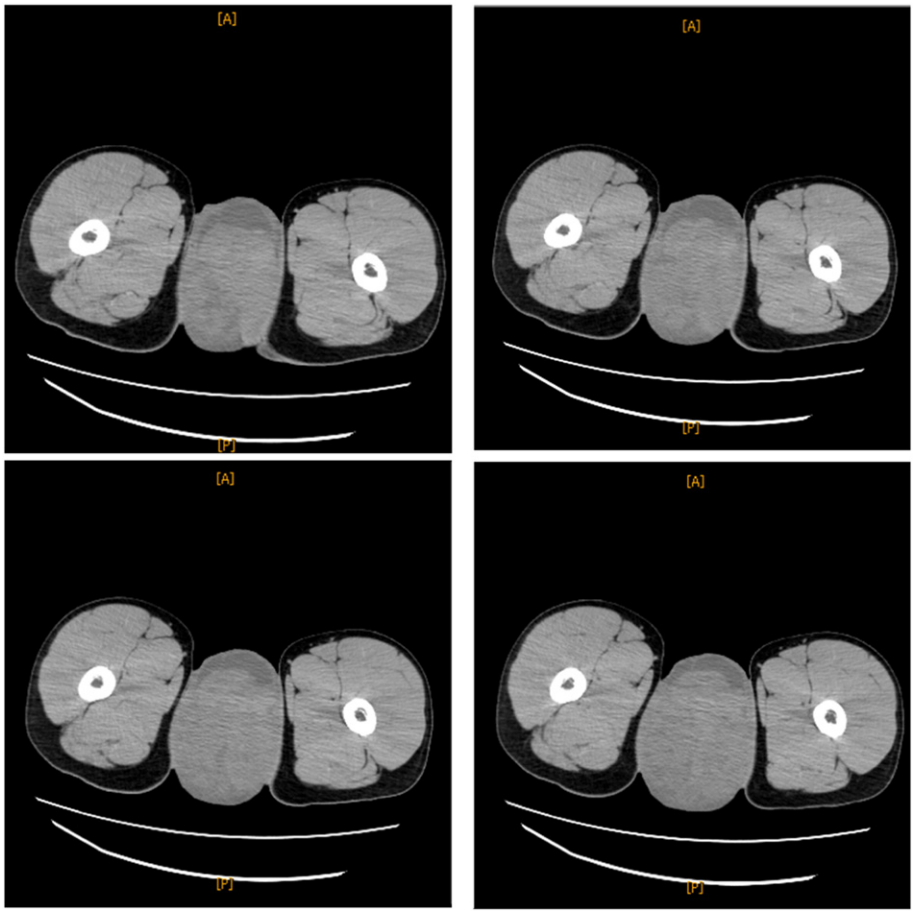

Fig. 3. A) The CT pictures of the root part of giant tumor, where yolk sac and embryonal carcinoma components were included. Clover like shades appeared in this lesion.

glypican 3 negative (Fig. 2G and H), and embryonal carcinoma component was glypican 3 positive and Oct4 negative (Fig. 2I and J).

The tumor testicular invaded into the epididymis, but did not invade into the ductus deferens. The tumor had vein permeations and lymphatic vessel permeations.

The computed tomography showed clover like structure at the sections where the embryonal carcinoma and seminoma were included (Fig. 3A).

3. Discussion

Rather a large part of the giant seminomas are diagnosed as pure seminoma in conventional histopathological examinations [4]. We had the question if giant seminomas are really composed of pure classic seminoma component. In addition, increase of AFP in the patient's blood also strongly suggested the inclusion of non-seminomatous components in this testicular tumor. Our results indicate that intensive histological examination may reveal the inclusion of other germ cell tumor elements in giant seminomas, which are recognized as pure classic seminomas through conventional histopathological examinations.

Obvious histopathological guideline does not exist for the slide numbers for giant seminomas. According to the AFIP's guideline, centimeter of tumor maximum dimension is the recommended block section number for large ovarian tumors. Similar standard might be adopted for histopathological examinations of large testicular tumors. But the standard may be insufficient for the detection of non-seminomatous elements. This case demonstrates that intensive histopathological examinations are recommended for large testicular tumors, especially for the cases with AFP and/or other blood marker elevations.

Intensive histopathological examination of giant testicular tumors may support accurate diagnoses and treatments. EP [etoposide and cisplatin] therapy is usually performed for pure seminomas. In contrast, BEP [bleomycin, etoposide, and cisplatin] or VIP therapy is performed for testicular tumors including non-seminomatous elements. Because the chemotherapy for testicular tumors with non-seminomatous elements is different from that for pure seminomas, histological detection of non-seminomatous elements is necessary for the appropriate treatments of testicular tumors.

This case suggests the possibility that non-seminomatous components have not been detected, because of the difficulties to detect them macroscopically.

Computed tomography (CT) pictures may help the histopathological examinations. Clover like structures which appear in CT pictures may be helpful for determining the tumor part selected for the histopathological blocks (Fig. 3).

Next we considered about the natural history of the tumor development. We were interested in how tumors change their characters during the development at the tumor origin [7]. Usual mixed type germ cell tumors consist of higher proportion of each component than this case, and macroscopic view is rather different from the pure classic seminomas [3]. This implies that mixed germ cell tumors originate from tumor initiating cells which have the potential to differentiate into different type germ cells. In contrast, the tumor initiating cells of seminoma, which have the restricted potential to differentiate into pure seminoma, are kept in the tumor.

This case included only tiny fragment of the embryonic carcinoma in among large component of classic seminoma (Fig. 2B). This case suggests that additional genetic changes might occur in the tumor initiating

cells of classic seminoma, and might convert into the other germ cell initiating tumor initiating cells, in the tumor origin, during the growth of the tumor. Leaving the tumor growth may increase the character changes of the tumor initiating cells of classic seminomas those with worse characters, which practically decide the prognosis [7].

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